UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,109	06/12/2001	Jacques Paris	GEI-073	6348

20311 7590 02/24/2003

MUSERLIAN AND LUCAS AND MERCANTI, LLP
600 THIRD AVENUE
NEW YORK, NY 10016

EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/423,109	Applicant(s) PARIS ET AL.	
	Examiner Sabiha Naim Qazi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *3-9, 11-13 and 18-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *3-9,11-13 and 18-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Acknowledgement is made of the response filed in paper no. 16. Claims 3-9, 11-13 and 18-30 are pending. No claim is allowed at this time.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Information Disclosure Statement

IDS is missing.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 18- rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is intended by "derivatives" in claims, see claim 18. Deletion of this term is requested.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-9, 11-13 and 18-30 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treating estrogenic deficiencies in menopausal women, does not reasonably provide enablement for the following.

a. Method "preventing estrogen deficiencies" and for "prevention of osteoporosis and cardiovascular disorders" as presently claimed.

b. Methods of treating or prevention by using "conjugated equine estrogens, esterified 17Beta estradiols, "estradiol derivatives" and nomagestrol or one of its esters".

Specification discloses an example III which is the combination of estradiol and nomgesterol acetate. In applicant's own disclosure on pages 6-11, it has been emphasized that the doses and amounts in the combination therapy is very important, various doses of estradiol and nomegetrols are known. Since as accepted prediction of several compounds and their combinations that would work the same way as estradiol and nomegestrol is impossible. Actually this is the same basis discussed in the disclosure by Applicants.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The nature of the invention:

The invention claims a method of treating estrogenic deficiencies in women comprising administering without interruption combination of a 0.5 to 3 mg of an estrogenic compound and 1.5 to 3.75 mg of nomegestrol acetate.

The predictability or unpredictability of the art

The unpredictability in the estrogen art is very high. The true fact of the state of the art in the hormone and steroid area for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study.

The breadth of the claims

The claims are very broad. See especially claims 18 and 19.

The amount of direction or guidance presented

The specification provides no guidance, in the way written description, to use the invention as claimed. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result.

The significance of particular combination of estradiol and nomegestrol cannot be predicted a priori but must be determined from the case to case by painstaking experimental study.

The presence or absence of working examples

There are no examples or test data to support the presently claimed invention containing the combination of the any other estrogen derivatives except example III that is the combination of estradiol and nomegestrol acetate. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The quantity of experimentation necessary

Since the nature of the method is so unpredictable, and since there is a lack of guidance present in the specification, the skilled artisan would have to undertake undue experimentation to practice the claimed invention commensurate with the scope of the claims. The skilled artisan, seeking lead

compounds for pharmaceutical discovery, would be at a loss as to where to begin such discovery in the absence of such data.

Since the significance of particular estrogen for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine the effect of the combination of all of the estrogen derivatives with nomegestrol derivative as presently claimed.

Claims are not limited to the scope to the extent of support in disclosure so that one skilled in the art without undue experimentation can practice invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patent ability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patent ability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3-9, 11-13 and 18-30 are rejected under 35 U.S.C. 103(a) as obvious over Plunkett et al. (US Re. 36,247) and Blanc et al. (Clinical Therapeutics, 1998), 20(5), 901-912). Both the references teach the art, which embraces instantly, claimed invention. See the entire documents.

1. Determining the scope and contents of the prior art.

Plunkett teaches a method of hormonal treatment for menopausal disorders involving continuous administration of progestogens and estrogens. See the entire document especially lines 40-51, col. 2; lines 63-67, col. 2; lines 1-67, col. 3; lines 18-25, and lines 1-5, col. 4; lines 46-50, col. 6.

The reference teaches continuous and uninterrupted administration of progestogen and estrogen. The actual unit dosage are selected according to conventionally known methods, e.g. body weight of patient and biological activity of hormones with the ultimate goal of producing the desired result with minimum quantities of hormones. It does not disclose specifically nomegesterol acetate.

Blanc et al teaches continuous hormone replacement therapy combining nomegesterol acetate and gel, patch or oral estrogen. See the abstract of the invention; cols 1 and 2 on page 903col. 2 on page 904Table 1 on page 905Figure on page 906 ; Table II on page 907. Prior art also teach that bleeding occurs when treatment is discontinued.

2. Ascertaining the differences between the prior art and the claims at issue.

Instant claims are drawn to a method of treating deficiencies of estrogen by continuously administering a combination of estrogen and nomagesterol acetate. Blanc et al. teach the same combination, the ranges of the amounts overlap with the prior art teaching. Prior art teaches estradiol, 2 mg/dose whereas presently claimed amount is 0.3-3 mg and nomegesterol 2.5 mg/d whereas presently claimed amount 0.3 to 1.25 mg. The Plunkett et al differs from the instant invention in that it does not specifically name nomegesterol acetate. Presently claimed invention does not clearly state what is the amount of the steroids per dose per day.

3. Resolving the level of ordinary skill in the pertinent art.

It would be obvious to one skilled in the art at the time of invention to prepare a composition to administer continuously combination of estrogen and nomegesterol as cited above.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Motivation is to use estrogen and progestogen continuously as taught by Plunkett et al. and use nomegesterol as progestagen because it gives in all patients regular, progestogen-induced withdrawal bleed each month; and histological, ultra structural and biochemical changes were induced within the endometrium by all doses (0.5 mg, 1.0 mg; and 2.5 mg) is a potent progestogen. Blanc et al. Teach same combination as combination of nomegestrol and estradiol. Thus, there has been ample motivation provided by the teachings of both the references cited above to prepare the instant invention in absence of any criticality or unexpected results.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Telephonic Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Naim Qazi whose telephone number is 703-305-3910. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER

February 23, 2003